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ORAL MALIGNANT MELANOMA: A CASE REPORT

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ABSTRACT
The oral malignant melanoma (OMM) is a rare disease, accounting for 0.8% of all melanomas and 8% of head and neck melanomas and up to 0.5% of all oral malignancies in the world literature. This presents as a pigmented lesion with asymmetrical borders, irregular surface characteristics and distinct color. Moreover melanoma associated pigmented lesion of the oral cavity does not possess clinical specificity and divert the clinical diagnosis, so differential diagnosis becomes mandatory to explore it. The most unpredictable pathophysiological behavior and late detection, contributes for bad prognosis of the disease. As a result, the 5 years survival rate is 10% to 25%. Commonly it is seen with maxillary gingiva of males. However we report a case of a middle aged female having pigmentations and growth over mandibular gingiva.

INTRODUCTION

Spontaneous efforts by researchers and day by day addition of literatures minimized the aura of one of the deadly disease, Oral malignant melanoma (OMM). As a result the new innovative approaches came to existence and this was time for first step success against this disease. The disease is known since decades, but the proper management is affected due to insufficient literature regarding its pathophysiology. Looking at the older literatures moreover, it attributes as a deadly unsolved mystery. Later on many authors contributed to solve the puzzle. In 1856, the mucosal melanoma was discussed first time by Weber in Germany, and later on, the valuable information of head and neck mucosal melanoma was reported by Lincoln in 1885. In late nineteenth century, further studies were carried out, that focused to minimize the mortality and enhance public awareness towards the disease. Hence an early detection and timely treatment is a key factor for its better prognosis. Apart from oral melanoma there is a marked variation in its generalized cutaneous counterpart, etiology and incidence rate. The continuous global environmental changes results over exposure for UV radiation. Similarly the growing trends of sun beds or tanning beds increased the risk of this disease. The sun bed is a device; which emits ultraviolet radiation (typically 97% UVA and 3% UVB, +/- 3%) to produce a cosmetic tan. Today the worldwide incidence of newly diagnosed melanomas ranges between 3-8% and around 50% of mucosal melanomas affect head and neck region; almost representing 9% of all malignant head and neck tumors. Comparatively mucosal melanomas show aggressive biological behavior resulting less than 25 % 5-year survival rate [1].

The etiology of mucosal melanoma differs from cutaneous counterpart, as there is no direct role of ultraviolet radiation. Primary causes are; ill fitting dentures, betel nuts, tobacco, formaldehydes, amalgam tattoo, nevi at traumatic regions and racial pigmentation etc [2]. Some literatures explain that; during embryologic development, melanocytes migrate from the neural crest to epithelial lining which later show reactive changes by cytotoxic stimulant in the basal epithelial layer [3]. Though dendritic cells, derived from neural crest produce the melanocytes but exact mechanism of proliferation of these cells in melanoma is not known.

Particularly mucosal melanomas are asymptomatic in their initial phase, resulting late diagnosis,

which usually invade in deeper regions. Moreover clinical characteristics includes, dark brown or black color, irregular surface and asymmetrical margins etc. So the pigmented lesions of oral cavity; which does not possess clinical specificity should be viewed with suspicion. It should be differentiated from other oral pigmented lesions; including drug pigments, smoke related melanosis, melanotic macule, Kaposi's sarcoma, physiologic or racial pigmentation, nevus and melanoacanthoma.

Pigmentation is not the only criteria, as around 15% of the melanomas are non pigmented and are typically red lesions, thus presenting as amelanotic melanoma, resembling red lesions. The OMM has distinct gender variation majority of them showing male predominance. Amongst the oral melanomas; hard palate and maxillary gingivae are common sites. The lesion is rarely documented in female patients. Location wise; the involvement of mandibular gingivae is comparatively less [4]. Here we report a case of OMM, in a 45 years old female patient , who is conscious about the discoloration and growing bulk over mandibular anterior mucosa.

CASE REPORT

A 42 years old Indian lady; with average height and moderate built reported to dental office, complaining of blackish discoloration on the lower jaw since 6 months and difficulty while eating; especially with the lower front teeth. Intraoral examination revealed non tender and painless; bluish black growth with rough and irregular surface extending over the gingiva of 35 to 44 region, which revealed no findings of ulceration and bleeding. (Fig.1) There was major involvement over the labial aspect of mandibular gingivae followed by anteroposterior extension into the vestibule and oral aspect of lip mucosa; but with minimal extension of the lesion on lingual aspect. The patient noticed a small blackish patch approximately 1x1 cm which gradually increased to present size with associated mobility of teeth. The mobility was appreciable in almost all mandibular anterior teeth. However except nevi; overall examination of neck, back, extremities and chest was insignificant, so the cutaneous part of melanoma was ruled out. During general examination, submandibular lymph nodes were nontender and enlarged; 1.5×1.5 cm in dimension. No history of trauma and tobacco habit was reported. All vital signs were within normal limits. After evaluating hematological parameters, incisional biopsy was performed under local anesthesia, for confirm diagnosis. In microscopic examination, the H & E stained section revealed insitu melanotic pigment growth. (Fig.2) The section showed large cells with pleomorphic vesicular nucleus and brown pigment, few abnormal mitoses and altered nucleocytoplasmic ratio, invading into the connective tissue, in the form of sheets, cords and islands. (Fig.3) The tissue was also Immunohistochemically stained for HMB-45, a specific marker for melanocytes that also revealed cytoplasmic positivity of malignant melanocytes for the antibody. (Fig.4, 5) After confirmed diagnosis as malignant melanoma, segmental resection and bone grafting was performed by medical personnel. In post treatment follow up, patient reported with some other problems like difficulty in eating and speech. The intraoral examination revealed uneven healing of resected part and further development of the bluish black patch on left posterior mandible; due to severe trismus and discomfort; post operative photograph was not taken. The lady was advised to visit our office in next follow up, but unfortunately she never turned back.

Figure 1. Clinical photograph showing bluish black irregularly spreading growth extending from mandibular left second premolar to right firstpremolar

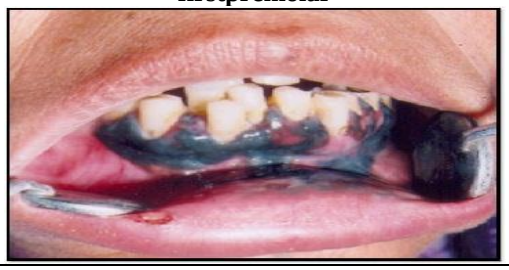


Figure 2. H and E stained section reveals malignant melanocytes with hyper chromatic nuclei; infiltrating the connective tissue as sheets. (H & E, 10X)

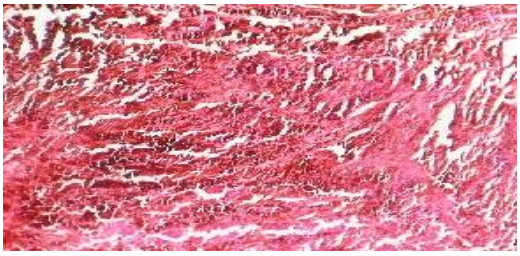


Figure 3. H and E stained section reveals pigmented cells with abnormal mitosis. (H & E, 10X)

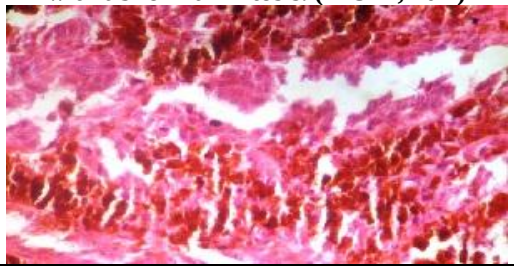


Figure 4. IHC stained slide shows positive expression. (IHC,10X)

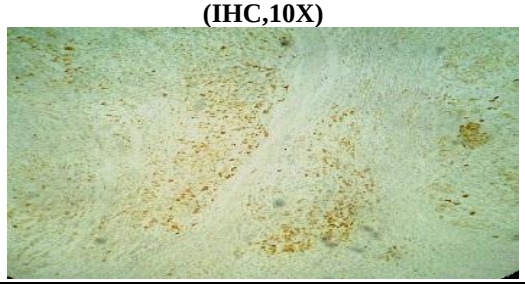
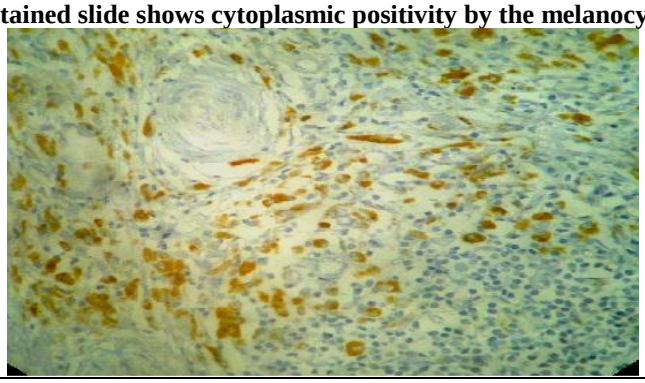


Figure 5. IHC stained slide shows cytoplasmic positivity by the melanocytes. (IHC, 40X)



DISCUSSION

The oral mucosal melanoma is a rare entity with incidence rates of less than 1% of all melanomas and amongst head neck tumors it is 1.6% .The worldwide incidence rate is up to 0.5% [5]. According to Andersen et al, the head and neck mucosal melanomas accounted for 0.8% of all melanomas and 8% of head and neck melanomas. They reviewed 2.5 million individuals in Denmark over a 30 year period and found that OMM mostly occur between the fourth and seventh decades of life, with a mean age of 55-57 years. It shows vague gender predilection accounting male to female ratio 3:1. The etiopathogenesis is still unknown; but even after its diverse nature, it is clear that, mucosal melanoma originates from melanocytes present in the mucosa. These are dendritic cells that have migrated as neuroectodermal derivatives in the ectodermally derived mucosa [3].

Some studies also suggest familial inheritance specially, along with dysplastic nevus syndrome where; p16 and differences in DNA repair impairments contributes to carcinogenesis of malignant melanoma. In such circumstances the damaged DNA, activates the proto-oncogenes or inactivates the tumor suppressor genes [6]. Majority of patients show history of pre-existing oral pigmentation before the diagnosis of oral melanoma. Moreover common primary sites include; the nasal cavity, para- nasal sinuses and in the oral cavity; maxillary alveolar ridge and hard palate, whereas it is rarely seen on the mandibular gingiva [7]. So far some studies have documented, relationship between free radicals, and melanoma cells, resulting into increase levels of reactive oxygen species (ROS). This is due to the metal binding properties of melanin and loss of structural integrity of melanosomes [8].

Presently it is accepted that, OMM is very aggressive tumor, and various factors contribute to its aggressiveness, such as late detection, poor resectability and early metastasis. This not only limits the 5 year survival rate up to 10-25%, but also affects prognosis. Melanoma is notoriously resistant to chemotherapy, but the other approaches can be carried out during its treatment. According to oncosurgeons; treatment of choice for malignant melanoma is surgery. Stage 1, melanomas are excised along with 1mm margins and T2aN0M0 (Stage 1 B) needs sentinel lymph node biopsy, and stage 2 cases are treated with wide excision and node biopsy. Whereas for stage 3 it needs wide excision with 2mm margins and node dissection and the radiation or chemotherapy is given postoperatively. Stage 4 is really the challenge; and along with surgery various parameters are added to it such as, chemotherapy, interferons, interleukins, vaccines and different biochemotherapeutic agents. Today's new technology has opened new hopes. As a result biotherapies including IFNs and IL-2 provide intriguing avenues for further study and treatment. The mechanism of clinically effective IL-2 therapy may be the direct action of IL-2 on a biologically distinct subset of melanoma cells, leading to up regulation of the tumor suppressor IL-24 [9].

The favorable prognosis of the lesion lies in its early diagnosis. Hence to avoid future complications the suspected oral pigmentations should be planned for biopsy. Moreover in some extent; GREENE criteria may be helpful to clinicians, that suggests; demonstration of melanoma in the oral mucosa, presence of junctional activity, inability to demonstrate extra oral primary melanoma.

Further some studies have classified the disease for prediction of its prognosis, i.e. Stage-I: when lesion is confined locally, Stage- II: have positive metastasis and Stage- III: with hematogenous spread. In late stage; distant metastases may be found in variety of sites, including the lungs, bones, liver brain and skin.

CONCLUSION

A detail case history, thorough clinical examination and suspicious eye to the irregular intraoral pigments can help the clinician for early diagnosis. Sometimes patients ignore the symptoms that may reflect indirectly on health care provision and result in a poor prognosis. Any physiologic pigmentation to hormones, medication or pigmentations other than amalgam tattoo should be biopsied. The treatment promoted by thorough oral examination and biopsy should be well planned to improve patient prognosis and avoid chances of recurrence.

Conflict of interest: NIL

REFERENCES

1. Papaspyrou G, Garbe C, Schadendrof D, Werner JA, Hauschild A, Eqberts F. (2011). Mucosal melanomas of the head and neck, new aspects of the clinical outcome, molecular pathology and treatment with C-kit inhibitors. *Melanoma Res*, 21, 475-82.
2. Bentham G, Aase A. (1996). Incidence of Malignant Melanoma of the skin in Norway, 1955-1989, Associations with Solar Ultraviolet Radiation, Income and Holidays abroad. *Int J Epidemiol*, 25, 1132-8.
3. Ardekian L, Rosen DJ, Peled M, Rachmiel A, Machtei EE, el Naaj IA, Lauffer D. (2000). Primary gingival malignant melanoma. Report of 3 cases. *Journal of Periodontology*, 71, 117–20.
4. Rapini RP, Golitz LE, Greer RO, Jr Krekorian EA, Poulson T. (1985). Primary malignant melanoma of the oral cavity. A review of 177 cases. *Cancer*, 55, 1543-51.
5. Hashemi P, Bujas T, Tomic K, Pericbalja M, Balicevic D, Kruslin B. (2006). Gastrointestinal melanoma review of computer data base in the period of 1996-2005. *Acta Clinica Croatica*, 45, 153.
6. Waldmann V, Bock M, Jackel A, Deichmann M, Dockndroff K, Naher H. (1999). Pathogenesis of malignant melanoma, molecular biology aspect. *Hautarzt*, 50, 398-405.
7. Lee SP, Shimizu KT, Tran LM, Juillard G, Calcaterra TC. (1994). Mucosal melanoma of the head and neck, the impact of local control on survival. *The Laryngoscope*, 104, 121-6.
8. Trapp V, Lee K, Donate F, Mazar AP, Fruehauf JP. (2009). Redox- related antimelanoma activity of ATN-224. *Melanoma Res*, 19, 350-60.
9. Emily YJ, Nancy JP, Elizabeth SF, Elizabeth AG. (2012). IL-2 regulates the expression of the tumor suppressor IL-24 in melanoma cells. *Melanoma Res*, 22, 19-29.